REMARKS

I. Status of the Claims

Claims 1-3, 5-6, 9-11, 17-21, and 23 remain pending in this application. Claims 4, 7, 8, 12-16, 22, and 24-33 have been canceled without prejudice or disclaimer. Claim 17 has been allowed. Claims 1, 20, 21, and 23 have been amended to excise certain groups from the definition provided for each of the groups Xa, Xb, Xc, Ya and Yb in the claims. These amendments only narrow the previously supported claims for purposes of advancing prosecution. Accordingly, no new matter has been introduced. 37 C.F.R. 1.121(f).

II. Applicants' Response to the Claim Rejections

Claims 1-3, 5-6, 9-11, 18-21, and 23 have been rejected under 35 U.S.C. 112, first paragraph. *Office Action* at 2-8. Claims 20, 21, and 23 have been separately rejected under 35 U.S.C. 112, first paragraph. *Office Action* at 8-15. Claims 1-3, 5, 9, 11, 18, and 19 have been rejected under 35 U.S.C. 102(a). *Office Action* at 15. Applicants respectfully submit that each of the above rejections should be withdrawn in view of the following remarks.

A. The Rejection of Claims 1-3, 5-6, 9-11, 18-21, and 23 Under 35 U.S.C. 112, First Paragraph Should be Withdrawn.

Applicants respectfully request that the Examiner withdraw the rejection of claims 1-3, 5-6, 9-11, 18-21, and 23 under 35 U.S.C. § 112, first paragraph because the specification enables the full scope of these claims. The Examiner has rejected each of claims 1-3, 5-6, 9-11, 18-21, and 23 because she believed that the specification did not

enable the full breadth of these claims. *Office Action* at 2-3 ("The specification does not enable . . . the invention commensurate in scope with these claims.").

Determining whether a particular claim is supported by the disclosure in an application requires determining whether that disclosure, when filed, contained sufficient information regarding the subject matter of the claims as to enable one skilled in the pertinent art to make and use the claimed invention. MPEP 2164.01. The test for enablement is whether the experimentation needed to practice the invention is undue or unreasonable. *Mineral Separation v. Hyde*, 242 U.S. 261, 270 (1916).

Applicant's specification enables a person having ordinary skill in the art to make the claimed compounds because the multiple alternative synthetic methods disclosed would not require undue experimentation to make the claimed compounds. The Examiner indicates that, because Applicants' specification does not specifically detail where to buy (or how to synthesize) each specific starting material and intermediate, the claimed compounds are not enabled. *Office Action* at 2-3. Applicants understand from the Examiner's remarks that she is concerned that the specification would not provide the claimed compounds if the materials required to make them were prohibitively unavailable. *See, e.g., id.* at 4-5. In support of her position, the Examiner cites, *inter alia*, *In re Wands, In re Fischer, Plant Syst. v. DeKalb Genet.* as standing for the proposition that starting materials must be explicitly provided. *Office Action* at 5-6. These cited cases, and the legal rational therein, relate to biotechnology inventions, and were decided at a time when biotechnology was in its infancy. In those cases, particular strains of starting materials (*e.g.*, microorganisms) were key to reproducing the

invention. This importance was due, in part, to the degeneracy of the genetic code and unpredictability as to what the starting materials actually were.

The MPEP discusses situations in which starting materials may present a "key issue" for enablement, pointing to cases where a particular biological strain or apparatus may not be available without extensive screening. MPEP 2164.01(b). Even in the biologics cases cited by the Examiner, it is settled that "as long as the specification discloses at least one method for making and using the claimed invention that bears a reasonable correlation to the entire scope of the claim, then the enablement requirement of 35 U.S.C. 112 is satisfied." MPEP 2164.01(b) (citing *In re Fisher*, 427 F.2d 833 (CCPA 1970)). Here, Applicants' synthetic procedures can not present an enablement problem because they involve small molecules, not biologics. Contrary to microorganisms and degenerate genetic material, small molecules present no challenge to those skilled in the art in determining what they are. Analytic techniques allow for precisely, accurately characterizing such compounds. Accordingly, the legal precedent upon which the Examiner bases her rejection should not apply to the starting materials and intermediates in this application.

Notwithstanding the inapplicability of the case law relied upon by the Examiner, the Examiner has also overlooked the fact that Applicants have provided synthetic instructions for synthesizing the starting materials and intermediates in question. In rejecting the claims for lacking enablement, the Examiner suggests that, even though the syntheses of the *claimed* compounds are sufficiently enabled, the starting materials may not be readily available. *Office Action* at 2-3. In particular, the Examiner asserts that "the specification fails to teach the commercial availability of or how to make all

necessary starting compounds (II), (III), (I-2), (I-4), (I-5), (V), (VI), (VIII), (IX), (X), (X1), (XIII), (XIV), (XV), (XVI), and (XIX)...." *Id.* In view of this premise, the Examiner concludes that the specification enables "only certain of the compounds of Formula I," *id.*, and states that "*[u]nless Applicants can provide reference to all of the necessary starting materials and procedures* required to make all of the compounds encompassed by claims 1-3, 5-7, 9-15, 18-21, 23 and 31, these claims must be limited to the supporting disclosure." *Id.* at 3 (emphasis added to show information requested). As described below, Applicants *have provided reference to all of the necessary starting materials and procedures* required to make the compounds encompassed by the pending claims. Accordingly, Applicants request that the Examiner withdraw the rejections under § 112, first paragraph and allow these claims.

The specification provides reference to and instructions for making the compounds of interest to the Examiner at least at the following parts of the specification, tabularized for clarity below:

Compound	Exemplary Enabling Disclosure
II	page 77, lines 3-6
III	page 77, lines 3-6
I-2	page 78, lines 9-11
I-4	page 79, lines 30-32
I-5	page 78, lines 12-17
V	page 84, lines 10-14
VI	page 84, line 13 - page 85, line 4
VIII	page 86, line 30 - page 88, line 4

IX	*see, e.g.*, VIII
X	page 88, line 5 - page 90, line 28
XI	page 93, line 6 - page 94, line 13
XIII	page 94, line 14 - page 95, line 7
XIV	page 95, lines 17-22
XV	page 95, lines 17-22
XVI	page 97, line 25 - page 98, line 7

Applicants have provided explicit disclosure of synthetic methods for preparing the claimed compounds. Applicants have also disclosed how to make the starting materials and intermediates which may be used to perform the synthesis of the claimed compounds. Accordingly, Applicants submit that claims 1-3, 5-6, 9-11, 18-21, and 23 are enabled and respectfully request that the Examiner withdraw the rejection of these claims under 35 U.S.C. 112, first paragraph.

B. The Rejection of Claims 20, 21, and 23 Under 35 U.S.C. 112, First Paragraph Should be Withdrawn.

Applicants request that the Examiner withdraw the rejection of claims 20, 21, and 23 under 35 U.S.C. 112, first paragraph. The methods of claims 20, 21, and 23 are enabled by the specification and the Examiner has not met the burden of refuting the objective truth of the specification.

As discussed above, the enablement requirement under 35 U.S.C. 112, first paragraph stipulates that the specification must describe how to make and use the claimed invention without undue experimentation. MPEP 2164; *see supra* at A. The Examiner "has the initial burden to establish a reasonable basis to question the enablement provided for the claimed invention." MPEP 2164.04 (citing *In re Wright*, 999

F.2d 1557, 1562 (Fed. Cir. 1993)). Where the art recognizes standard modes of administering a chemical compound, the specification need only provide a *connotation* of how to use the claimed compounds in order to meet the enablement requirement. MPEP 2164.01 (emphasis added). For example, "it is not necessary to specify the dosage . . . if it is known to one skilled in the art that such information could be obtained without undue experimentation." *Id.*

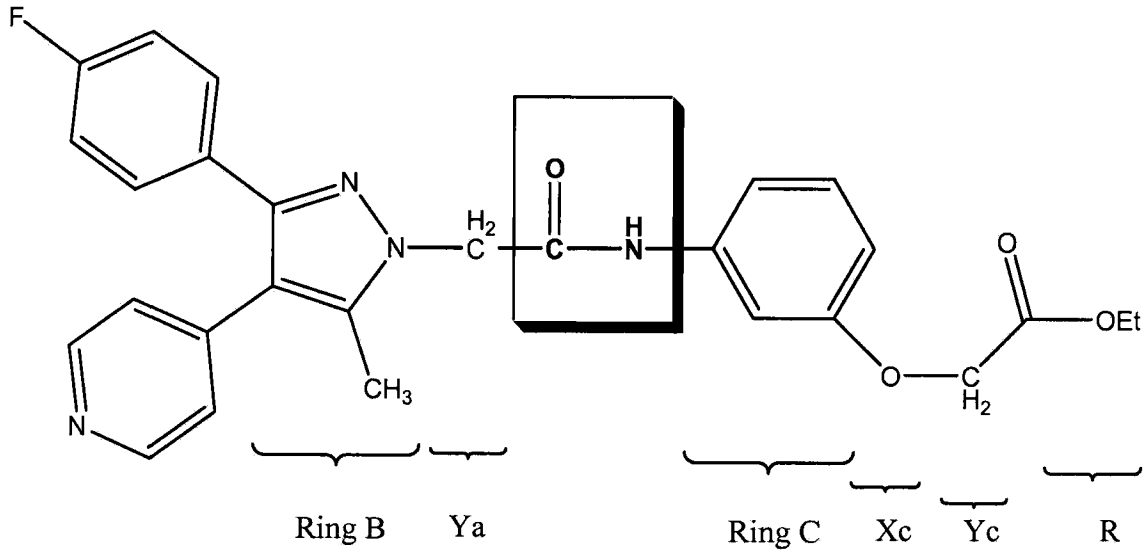
The specification provides an enabling disclosure for each of the methods claimed because it expressly discloses how the disclosed compounds should be administered to treat specific diseases. Each of claims 20, 21, and 23 is to a method of treatment. Claim 20 is to a method of treating type 2 diabetes. Claim 21 is to a method of treating hyperlipidemia. Claim 23 is to a method of treating impaired glucose tolerance (IGT). The specification provides for compounds which may be used to treat type 2 diabetes, *see supra*, and also expressly teaches using those compounds as "an agent for ... treatment of ... type 2 diabetes... hyperlipidemia ... impaired glucose tolerance (IGT)...." *Specification* at 62. The specification describes how to diagnose diabetes. *See, e.g., id.* at 62-63. The specification also outlines how the compound may be dosed within the disclosed methods of treatment. *See id.* at 67-68. As one of ordinary skill in the art would recognize, the specific dose used would depend on the patient's particular situation, *e.g.*, "depending on administration subject, administration route...," etc. *Id.* at p. 67. Accordingly, the general guidelines in the specification provide a person of ordinary skill with ample guidance for using the methods claims 20, 21 and 23.

While the specification only needs to provide "a *connotation* of how to use the claimed compounds in order to meet the enablement requirement," MPEP 2164.01, Applicants have provided *explicit guidance* as to how to use the compounds. Applicants have identified particular diseases, exemplified how to diagnose them, and provided general outlines for administering the compounds to subjects in need of treatment. Such disclosure fulfills the enablement requirement and the Examiner has not met her "initial burden to establish a reasonable basis to question the enablement provided for the claimed invention." MPEP 2164.04 (citing *In re Wright*, 999 F.2d 1557, 1562 (Fed. Cir. 1993)). In view of Applicants' enabling disclosure and the Examiner's failure to meet the burden for disputing it, Applicants' respectfully request that the Examiner withdraw the rejection of claims 20, 21, and 23 under 35 U.S.C. 112, first paragraph.

C. Claims 1-3, 5, 9, 11, 18 and 19 are Not Anticipated by the '977 Patent.

With entry of the amendments in this paper, claims 1-3, 5, 9, 11, 18 and 19 are not anticipated by U.S. Patent No. 6,514,977 (the "'977 patent"). As the Examiner points out, 35 U.S.C. 102(a) bars patentability of claims previously patented or described in a printed publication before an applicant's invention. *Office Action* at 15 (citing 35 U.S.C. 102(a)). Here, with entry of the amendments in this paper, the '977 patent does not describe the claims rejected by the Examiner because the compound cited by the Examiner does not fall within the compounds claimed in this application. For example, the compound cited by the Examiner has a $-CH_2-C(O)-NH-$ moiety bridging the pyrazolyl portion of the molecule (compare ring B) to the phenyl (compare ring C). The amended claims require that ring B bridges to ring C through a C_{1-16} alkylenyl- or C_{2-6} alkynyl- ether (Xa = bond; Xb = O; Ya = C_{1-6} alkylenyl- or C_{2-6} alkynyl- ;

and Yb= bond). As depicted below, the compound cited by the Examiner cannot meet this limitation.



In the above-depicted figure, selections were made for each of Ring B, Ya, Ring C, Xc, Yc, and R in the claimed compounds in an attempt to generate the compound cited by the Examiner. However, the claimed compounds cannot overlap with the compound cited by the Examiner for at least the reason that the claimed compounds do not have either of a bridging carbonyl or an amino group (together forming the amide group boxed in the figure above). In addition to this difference, the compound cited by the Examiner would not meet other limitations of Applicants' claims, such as, for example, (1) the C_{1-16} alkylenyl- or C_{2-6} alkynyl- ether moiety required in all of Applicants' compounds or (2) the oxygen atom in the bridging group, required by Xb, in all of the claimed compounds. The compound of the '977 patent cited by the Examiner does not fall within the compounds recited in claims 1-3, 5, 9, 11, 18 and 19. Accordingly this compound does not anticipate Applicants' claims. Applicants

respectfully request that the Examiner withdraw the rejection of claims 1-3, 5, 9, 11, 18 and 19 under 35 U.S.C. 102(a) because these claims are not anticipated.

III. Conclusions

Applicants respectfully request that the Examiner withdraw the rejection of claims 1-3, 5-6, 9-11, 18-21, and 23 under 35 U.S.C. 112, first paragraph. *See Office Action* at 2-8. These claims are enabled by the specification because the specification discloses how to make and use the claimed compounds. Additionally, while not necessarily required to satisfy the enablement requirement in this case, Applicants have also disclosed how to synthesize the starting materials and intermediate compounds.

Applicants respectfully request that the Examiner withdraw the rejection of claims 20, 21, and 23 have under 35 U.S.C. 112, first paragraph. *See Office Action* at 8-15. These claims, directed to methods of treatment, are enabled by the specification because the specification discloses the compounds used in the claims, the diseases treated in the claims, methods for diagnosing such diseases, and guidelines for administering appropriate dosages.

Applicants respectfully request that the Examiner withdraw the rejection of claims 1-3, 5, 9, 11, 18, and 19 under 35 U.S.C. 102(a). The compounds recited in these claims cannot overlap with the compound in the '977 patent cited by the Examiner because (a) the compound cited by the Examiner does not include moieties required by the compounds recited in the claims and (b) the compounds recited in the claims must include moieties not present in the compound in the '977 patent cited by the Examiner.

In view of the above remarks, prompt and favorable reconsideration of this application is requested, together with a timely notice of allowance.

Please grant any extensions of time required to enter this response and charge any additional required fees to our deposit account 06-0916.

Respectfully submitted,

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